

Message Text

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FOR OES/APT/BMP, MR. WALSH

DEPT PASS TO DHEW/OIH, DR. KING; NIH/NCI, DR. OMATA

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SUBJECT: USE OF PROTOPORPHYRIN IN CANCER THERAPY

REF: TOKYO 8452, STATE 149650

1. APPOINTMENT WAS ARRANGED WITH DR. IJIMA AS SOON AS POSSIBLE AFTER RECEIPT OF STATE REFTEL. SCIOUNS VISITED DR. IJIMA AT ST. MARIANNA ON JULY 9, ACCOMPANIED BY DR. YOJI IKAWA, JAPANESE SECRETARY OF US/JAPAN COOPERATIVE CANCER RESEARCH PROGRAM.

2. DR. IJIMA IS SENIOR RESEARCH PHYSICIAN FORMERLY WITH DEPT. OF SURGICAL RESEARCH, INSTITUTE OF MEDICAL SCIENCE, UNIVERSITY OF TOKYO, WHERE HE WORKED UNDER PROF. Y. ISHIBASHI (LEADING CANCER SPECIALIST IN JAPAN). MUCH OF IJIMA'S RESEARCH APPEARS TO HAVE BEEN DEVOTED TO CELL REGULATORY PROCESSES, AND IN PARTICULAR TO ROLE OF PROTOPORPHYRIN (PP) IN SUCH PROCESSES. AMONG SERIES OF REPRINTS GIVEN TO SCICOUNS (REPRINTS IN JAPANESE AND ENGLISH BEING POUCHED TO WALSH FOR DELIVERY TO NCI), IS A PAPER PUBLISHED IN 1968 ENTITLED "EFFECT OF PROTOPORPHYRIN UPON EXPERIMENTAL PORPHYRIA IN RATS". IJIMA SAYS HIS CURRENT LINE OF RESEARCH WAS STIMULATED BY TWO PAPERS PUBLISHED IN BRITISH JOURNAL OF SURGERY: (A) "THE ROLE OF CELLULAR IMMUNITY IN CONTROL OF NEPLASIA", G. BONE AND R. CAMPLEJOHN, VOL. 60, 824-827 (1973); (B) "MEASUREMENT OF CELL PRODUCTION RATES IN HUMAN GASTROINTESTINAL CANCER - A GUIDE TO TREATMENT?", D.C.

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BRITTON, G. BONE, N.A. WRIGHT, AND R.S. CAMPLEJOHN, VOL. 62,

813-815 (1975). ALTHOUGH WE DID NOT HAVE CAHNCE TO READ THESE PAPERS, THEY APPEAR TO DESCRIBE HUMAN TUMOR GROWTH RATE TO BE DIFFERENCE IN RATE OF GENERATION OF NEW CANCER CELLS AND RATE OF DISAPPEARANCE OF CELLS DUE TO CELL DEATH OR DISPERSAL. TUMOR GROWTH RATE IS EXPONENTIAL AND CHARACTERIZED BY DOUBLING TIME; CELL GENERATION RATE IS ALSO EXPONENTIAL WITH DIFFERENT TIME CONSTANT. AT SOME POINT, CELL PROLIFERATION RATE EXCEEDS RATE AT WHICH TUMOR MASS CAN GROW AND METASTASIS OCCURS. PURPOSE OF IJIMA RESEARCH IS TO INCREASE ABNORMAL CELL DEATH RATES WITHOUT AFFECTING NORMAL CELL METABOLISM. PP, AS NORMAL CONSTITUENT OF ANIMAL TISSUE, IS APPARENTLY INACTIVE IN THIS REGARD, BECAUSE IT IS BELIEFED TO HAVE BEEN RENDERED INACTIVE BY FORMATION OF COMPOUNDS WITH HEAVY METALS (E.G., ZN, PB) THAT OCCUR IN TRACE AMOUNTS IN TISSUE. THEREFORE, PP MUST BE ARTIFICIALLY ADMINISTERED.

3. INITIAL EXPERIMENTS WITH PP WERE PERFORMED ON CALF BOINE ERYTHROCYTES IN VITRO. THEN MOUSE HEPATITIS CELL LINE WAS CULTURED IN VITRO AND EFFECT OF TREATMENT BY PP ON CELLS PRIOR TO TRANSPLATATION TO C3H MICE WAS STUDIED. LAST SET OF MOUSE EXPERIMENTS USED C3H MICE WITH SPONTANEOUS MAMMARY TUMORS; ORAL ADMINISTRATION OF PP TO MICE WAS EFFECTIVE IF TUMOR DIAMETER HAD NOT EXCEEDED ONE CENTIMETER.

4. IN ADDITION TO CASE DESCRIBED TOKYO REFTTEL, IJIMA HAS A FEW OTHER HUMAN PATIENTS UNDER TREATMENT WITH PP. SOME ARE AFFLICTED WITH CANCER OF LARYNX. OTHERS ARE EITHER PRE- OR POST-OPERATIVE GASTRIC CANCER PATIENTS. HE WOULD PREFER TO TREAT EARLY GASTRIC CANCER CASES AFTER DIAGNOSIS BY FIBERSCOPE EXAMINATION AND BIOPSY, BUT PATIENTS ELECT SURGERY RATHER THAN TAKING CHANCE WITH CHEMOTHERAPY. THREE SUCH EARLY GASTRIC CANCER CASES ARE NOW UNDER PP TREATMENT. IJIMA SAYS THAT HE HAS ALMOST COMPLETED PAPER N HUMAN CLINICAL CASES AND WILL FORWARD DRAFT TO SCICOUNS AND DR. IKAWA IN ONE OR TWO WEEKS.

5. DR. IJIMA EXPRESSED CAUTION ABOUT SOURCE OF PP USED IN TREATMENT. HE USES COMMERCIALY AVALABLE DRUG MANUFACTURED BY FUJI SOKIN AND CALLED "PROT". PP MANUFACTURED BY A FIRM IN FRG HAS BEEN FOUND TO BE INEFFECTIVE, PERHAPS BECAUSE WRONG METALLIC COMPONENTS IS PRESENT. FURTHERMORE, PP APPARENTLY IS SOMEWHAT UNCLASSIFIED

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UNSTABLE. 20 COMPANIES IN JAPAN ARE NOW MARKETING PP FOR HEPATITIS TREATMENT. ORAL DOSE USED FOR HEPATITIS IS 6 TABLETS PER DAY (120 MG TOTAL, WHEREAS CANCER THERAPY DOSE IS ONE TABLERT PER DAY KWP MG). IJIMA IS CONVINCED THAT DRUG IS COMPLETELY SAFE SINCE NO SIDE FFECTS HAVE BEEN OBSERVED IN ANY HEPATITIS CASES TREATED. APPARENTLY IJIMA HIMSELF TAKES PP FOR HEPATITIS.

6. COMMENT: IT WAS SOMEWHAT DIFFICULT TO COMMUNICATE WITH DR. IJIMA BECAUSE, ALTHOUGH HE APPEARS TO UNDERSTAND ENGLISH,

HE PREFERS TO SPEAK IN JAPANESE. TRANSLATION OF HIS PAPERS WILL GIVE MORE ACCURATE ACCOUNTING OF HIS RESEARCH.

AN INTERESTING BUT OBVIOUS THOUGHT OCCURS TO US THAT IF THEORY OF CANCER CELL PROLIFERATION AND EFFICACY OF PP ARE CORRECT AS CITED BY DR. IJIMA, PP MIGHT QUALIFY AS CANCER "PREVENTATIVE". HUMAN POPULATION ALREADY TREATED WITH PP FOR HEPATITIS WOULD BE AVAILABLE FOR STATISTICAL EPIDEMIOLOGICAL STUDY. THIS MIGHT BE SUITABLE SUBJECT FOR CONSIDERATION BY US/JAPAN COOPERATIVE CANCER RESEARCH GROUP.

7. WHILE WE WERE AT ST. MARIANNA WE ALSO INQUIRED ABOUT WORK OF DR. TAKASHI YAMAMOTO, A COLLEAGUE OF DR. IJIMA WHO IS STUDYING THE EFFECT OF A DYE CALLED "PHYTOCHLORIN", ISOLATED FROM CHLOROPHYLL, AS A CANCER PREVENTATIVE. YAMAMOTO IS SAID TO HAVE GIVEN A PAPER ON HIS RESEARCH AT THIRD INTERNATIONAL SYMPOSIUM ON CANCER PREVENTION IN NEW YORK, MAY 26. YAMAMOTO WAS AWAY FROM UNIVERSITY DURING VISIT AND FURTHER INFO COULD NOT BE OBTAINED.

8. WE LEARNED FROM DR. IJIMA THAT THERE IS A RESEARCHER AT KYOTO PREFECTURAL MEDICAL COLLEGE WHO IS STUDYING THE USE OF ENZYMES IN CANCER THERAPY. NAME COULD NOT BE RECALLED. DR. CARBONE AT NCI HAS ASKED FOR INFORMATION ON THIS SUBJECT. WILL TRY TO LOCATE RESEARCHER.

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